REMARKS

Claims 1-22 are pending. Claims 1, 7-9, 14 and 15 have been amended and claims 12-13 have been cancelled.

Applicants have amended the sequence listing to correct typographical errors and to include the inadvertently omitted sequence identifier (SEQ ID NO:4) on page 7 of the published application as instructed by the Examiner. Please replace the previously filed sequence listing with the attached substitute sequence listing. No new matter is believed to have been added.

Rejection under 35 U.S.C. §112 second paragraph

The Applicants have amended claims 7-9 and 15 to address each of the Examiner's objections.

Rejection under 35 U.S.C §102

The Examiner has rejected claims 1, 9 and 11 as anticipated by Hashimoto et al. and also claim 1 as anticipated by Gray et al. Claim 1 has been amended to require contacting the sample with a first reagent comprising a chitin-binding domain (CBD) which is fused to a maltose-binding domain (MBD). Neither Gray et al. nor Hashimoto et al. suggest or teach the use of MBD. The Examiner is respectfully requested to reverse the rejection.

The Examiner has rejected claims 12 and 13 as anticipated by Idusogie et al. Applicants traverse this rejection. However, claims 12 and 13 have been cancelled. Claim 14 has incorporated the limitations of claims 12 and 13 and is now an independent claim. As such the Examiner's rejection is rendered moot.

Rejection under 35 U.S.C. §103

(1) The Examiner has rejected claims 1, 4, 5, 9, 11 and 12 as unpatentable over Tuse et al. in view of Hashimoto et al.

(2) The Examiner has rejected claims 2 and 3 as unpatentable over Tuse et al. in view of Gray et al.

(3) The Examiner has rejected claims 6-8 as being unpatentable over Tuse et al. in view of Hashimoto et al. and Gray et al.

(4) The Examiner has rejected claim 10 as being unpatentable over Tuse et al. and Hashimoto et al. in view of Harman et al.

(5) The Examiner has rejected claims 13 and 17 as being unpatentable over Tuse et al. and Hashimoto in view of Foster et al.

The present rejections of obviousness all rely on the Examiner's rejection of allowable claim 1 as obvious. However,

Applicants assert that claim 1 is allowable for the following reasons:

(1) Tuse et al. in view of Hashimoto for claims 1, 4, 5, 9, 11 and 12

Scope and content of the prior art and the differences between the prior art and the claims at issue

Tuse et al. utilize chitinase and not a chitin-binding domain to detect chitin-containing organisms. A problem with chitinase is that it cleaves chitin which is the substrate of the enzyme. It is also non-specific as noted in the application on page 3. The assays described by Tuse et al. were not enabled as no experimental data was provided, only cartoon figures. Applicants do not believe that the assay of Tuse et al. could work because of the use of chitinase. In addition, there is no suggestion in the cited references that a fusion protein should be used to specifically detect chitin that includes CBD and MBD as claimed in claim 1.

Applicants have used a chitin-binding domain which has been specifically defined on page 7 of the specification and which was demonstrated not to cleave chitin or bind cellulose (page 10 of the specification). Advantages of using the claimed fusion protein include increased solubility and avoidance of problems of aggregation. Additional advantages include ease of purification of CBD on an amylose column to which MBD binds and the use of MBD as a reporter. The above application describes how to position the MBD with respect to the CBD in

such a way as not to interfere with CBD binding to chitin (page 14 of the specification and Example1). None of the cited references alone or in combination suggest or teach how to make a fusion protein between CBD and a second protein more specifically MBD.

Hashimoto et al. recognize the problem of chitinase and describe the binding properties of a chitin-binding domain. However, Hashimoto et al. do not suggest the preparation of a conjugate as required in claim 1, in particular an MBD-CBD conjugate, nor that the conjugate might retain the favorable binding properties that Hashimoto et al. described for the chitin-binding domain nor that the conjugate could be effective in detecting chitin in a sample.

Evidence of skill in the art

In rejecting the claims as obvious, the Examiner recited 6 different references: Tuse et al. (1992), Hashimoto et al. (2000), Gray et al. (2002, filed 1999) Foster et al, (1984), Idusogie et al. (2001, filed 1998) and Harman et al. (2001, filed in 1991). These references were submitted over a period of 15 years. None of the references mention forming a conjugate of CBD with another protein let alone MBD. This would suggest that the method in claim 1 was not only novel but also non-obvious.

Additional rejections of obviousness

(2) Tuse et al. in view of Gray et al. for claims 2 and 3

Scope and content of the prior art and the differences between the prior art and the claims at issue

Claims 2 and 3 require the use of a reporter attached to the chitin-binding domain in the CBD-MBD conjugate for the claimed method of detecting chitin and not cellulose in a sample.

The Tuse et al. reference relies on chitinase, not a chitin-binding domain–MBD conjugate, and an antibody label. The Gray et al. reference describes the use of a human chitinase fragment product as a therapeutic agent adjunct.

> Specifically contemplated by the invention are compositions comprising chitinase fragment products for use in methods for treating a mammal susceptible to or suffering from fungal infections. (Gray et al. col 8, lines 34-37).

Gray et al. contemplate conjugating human chitinase fragment products to a variety of anti-fungal agents. The use of reporters is not suggested.

Evidence of skill in the art

Despite the plethora of references describing uses of chitinase and chitinase fragments cited by the Examiner, there was no suggestion of a method as presently claimed. It is respectfully submitted that it would merely be an exercise in hindsight to conclude that the present claimed invention in claims 2 and 3 is obvious in view of Tuse et al. and Gray et al.

(3) Tuse et al. and Hashimoto et al. in view of Gray et al. for claims 6-8.

Scope and content of the prior art and the differences between the prior art and the claims at issue

As discussed above, Tuse et al. describe the uses of chitinase and not a chitin-binding domain alone or fused to MBD. Hashimoto et al. describe the characterization of a chitin-binding domain but no use is suggested for this. Gray et al. describe therapeutic applications of human chitinase fragments. None of the references suggest a CBD-MBD fusion protein for use in detecting chitin and not cellulose.

Evidence of skill in the art

Despite the plethora of references describing uses of chitinase and chitinase fragments cited by the Examiner, there was no suggestion of a method as presently claimed. It is respectfully submitted that it would merely be an exercise in hindsight to conclude that the present claimed invention utilizing a fusion of two different proteins and use of a second reagent in claims 6-8 is obvious in view of the combined teaching of Tuse et al., Hashimoto et al. and Gray et al.

(4) Tuse et al. in view of Hashimoto et al. in view of Harman et al. for claim 10.

Scope and content of the prior art and the differences between the prior art and the claims at issue

As discussed above, Tuse et al. and Harman et al. describe the uses of chitinase and not a chitin-binding domain alone or fused to MBD. Hashimoto et al. describe the characterization of a chitin-binding domain but no use is suggested for this. None of the references suggest a CBD-MBD fusion protein.

Evidence of skill in the art

Despite the plethora of references describing uses of chitinase and chitinase fragments cited by the Examiner, there was no suggestion of a method as presently claimed. It is respectfully submitted that it would merely be an exercise in hindsight to conclude that the present claimed invention utilizing a fusion of two different proteins and bleaching the sample in claim 10 is obvious in view of Tuse et al., Hashimoto et al. and Harman.

(5) Tuse et al. and Hashimoto et al. in view of Foster et al. for claims 13 and 17. Claim 13 has been cancelled. Claim 17 is now dependent on amended claim 14 which the Examiner has found to be allowable if written in independent form. Hence, claim 17 should also be found allowable.

Scope and content of the prior art and the differences between the prior art and the claims at issue

As discussed above, Tuse et al. describe the uses of chitinase and not a chitin-binding domain alone or fused to MBP. Hashimoto et al. describe the characterization of a chitin-binding

domain but no use is suggested for this. Foster et al. describe an immunoassay with instructions. None of the references suggest a soluble CBD carrier protein fusion molecule linked to a reporter.

Evidence of skill in the art

Despite the plethora of references describing uses of chitinase and chitinase fragments cited by the Examiner, there was no suggestion of a kit as presently claimed in claim 17.

Summary

Applicants submit that the claims as amended are neither anticipated nor obvious over the cited references. The Examiner is respectfully requested to reverse the rejection of the claims.

CONCLUSION

Applicants respectfully submit that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited.

Applicants attach a petition for a three-month extension of time and authorize that $710, covering the extension fee and the fee for a multiple-dependent claim, be charged to Deposit Account No. 14-0740. Applicants authorize that any deficiencies be charged to Deposit Account No. 14-0740.

Respectfully submitted,

NEW ENGLAND BIOLABS, INC.

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/Harriet M. Strimpel, D.Phil./
Harriet M. Strimpel D.Phil.
(Reg. No.: 37,008)

Customer No.: 28986

Attorney for Applicant
240 Country Road
Ipswich, Massachusetts 01938
(978) 380-7373